REMARKS

Formal Matters

Claims 27-30 and 38-43 are pending after entry of the amendments set forth herein.

Claims 27-30 were examined. Claims 27-30 were rejected.

Claim 27 is amended to remove an accidental duplication of a phrase. In other words, one redundant copy of the phrase "wherein the TaHo protein is encoded by a nucleic acid having at least 90% identity to the nucleic acid sequence set forth in Figure 1 (SEQ ID NO:1) or Figure 2 (SEQ ID NO:2)", was deleted from the claim. That phrase is set forth only once in the amended claim.

No new matter is added by this amendment.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Specification

The Examiner has requested that the priority information contained in the first paragraph be updated.

The Applicants have updated this information.

Sequence compliance

The Examiner notes that the application fails to provide a SEQ ID NO for a sequence depicted on page 14.

The paragraph starting on line 25 of page 14 has been amended to recite a SEQ ID NO.

The Applicants respectfully submit that the specification is now in compliance with the sequence rules, and request withdrawal of this objection.

Claim objections

Claim 27 is objected to for having redundant phrases.

Without acquiescing to this rejection, claim 27 has been amended to remove one of the redundant phrases.

The Applicants respectfully submit that this objection has been adequately addressed, and, accordingly, this objection may be withdrawn

Rejections Under 35 U.S.C. § 112, ¶1 – Enablement

Claims 27-30 and 38-43 are rejected under 35 U.S.C. §112, first paragraph, because the specification assertedly fails enable the claimed methods. Specifically, the Office states that "A review of the scientific literature shows that PARP requires the presence of DNA, histones and Mg2+ for NAD hydrolyzing activity", and contends that the specification cannot enable the claimed PARP assays because it fails to teach those components of the assay. The Applicants respectfully traverse this rejection.

With respect to the question of enablement, the MPEP is explicit: a patent specification need not teach, and preferably omits, what is well known in the art.[1]

The Applicants agree with the Examiner in that certain references in the prior art may teach that DNA, histones and Mg^{2+} are required for PARP activity. In fact, prior to the filing date of the instant patent application, the Applicants respectfully submit that the art was replete with PARP assays containing DNA, histones and Mg^{2+}, and that these compounds were well known components of PARP assays. Support for this position is found in Koide (Biochem. Soc. Trans. 1973 1:644-648), Kristensen (Eur. J. Biochem. 1976 70:441-446) and Tsopanakis (Eur. J. Biochem 1978 90:337-345), as cited by the Office to establish the rejection under 35 U.S.C. § 102, as discussed below.

In view of the guidance regarding what is required for an enabling disclosure as set forth in the MPEP, because DNA, histones and Mg^{2+} were well known components of PARP assays, they need not be taught by, and in fact are preferably omitted from, the instant patent application. In other words, the law discourages applicants from describing in the specification that which was already known in the art; omission of the details of the well-known PARP assay is tantamount to omitting that which was already known in the art.

This rejection may be withdrawn without any further discussion.

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[1] MPEP at § 2164.01 "A patent need not teach, and preferably omits, what is well known in the art." citing *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Rejections Under 35 U.S.C. § 102

Claims 27-30, 38, 41-43 are rejected under 35 U.S.C. § 102(b) as being anticipated by Koide (Biochem. Soc. Trans. 1973 1:644-648), Kristensen (Eur. J. Biochem. 1976 70:441-446) or Tsopanakis (Eur. J. Biochem 1978 90:337-345).

The Office argues that each of the cited references describes the purification of PARP enzymes from several sources, and discloses PARP activity assays using the purified enzymes. The Office takes the position that the PARP activity assays described in the cited references inherently involve a protein that is encoded by a nucleic acid having at least 90% identity to SEQ ID NO:1 or SEQ ID NO:2, and, as such, has rejected the claims over the cited references. The Applicants respectfully disagree.

This rejection appears to be based on a theory of inherency. The MPEP at § 2112 provides very clear guidance for establishing such rejections:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.[2] (emphasis in the original).

In order for a rejection based on inherency to be correctly established, according to the MPEP, a claim limitation that is not explicitly taught must be inherent, i.e., necessarily present, in the cited prior art. The mere possibility that the limitation is taught in the art is not sufficient to merit such a rejection, and the mere fact that a certain thing *may* result from a given set of circumstances is also not sufficient.[3]

There are several PARP domain-containing proteins in a mammalian cell, including PARP1, PARP2, PARP3, VPARP, KIAA0177, ADPRT, NP_001609, the telomere associated proteins tankyrase (TANK1) and tankyrase H (TANK2), and many others. The Applicants respectfully submit that the Office has not set forth any reasoning why, out of all of the possible mammalian PARP proteins, Tankyrase H is the PARP protein present in Koide, Kristensen and Tsopanakis's assays. Tankyrase H is not necessarily the PARP protein purified by Koide, Kristensen and Tsopanakis, and, as argued below, is probably not. Accordingly, while the Office may argue that there is a *possibility* that the cited references

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[2] MPEP at § 2112, citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)

[3] MPEP at § 2112 "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed.

may have described a PARP assay containing Tankyrase H, the fact that such a possibility exists is insufficient grounds, according to the MPEP and current law, to reject the instant claims.

Further, the Applicants respectfully submit that the PARP protein purified by Koide, Kristensen and Tsopanakis is likely PARP-1 and not Tankyrase H. Until the late 1990's, it was generally thought that there was a single PARP activity in mammalian cells (see, e.g., the last paragraph of the discussion of Shieh et al., J. Biol. Chem. 1998 283:30069-30072), enclosed herewith as Exhibit A. In other words, at the time of publication of Koide (1973), Kristensen (1976) and Tsopanakis (1978), there was only recognition of a single PARP enzyme (called "PARP"), and no recognition of any other enzymes with poly(ADP-ribose) polymerase activity in mammalian cells. The Applicants respectfully submit that the PARP enzyme studied by Koide, Kristensen and Tsopanakis was purified to homogeneity, cloned and sequenced by Kurosaki et al. (J. Biol. Chem. 1987 262 15990-15997, enclosed herewith as Exhibit B). The protein described in Kurosaki et al. has been named "PARP-1" (see Genbank record enclosed herewith as Exhibit C). As evidenced by a sequence alignment attached hereto as Exhibit D, the PARP-1 cDNA exhibits 46.0% and 46.3% sequence identity to SEQ ID NO:1 and SEQ ID NO:2 respectively. These sequence identities are considerably less than the 90% sequence identity required by the rejected claims.

In other words, the Applicants respectfully submit that the assays described in Koide, Kristensen and Tsopanakis involve PARP-1. Because of this, the Applicants respectfully submit that the teachings of Koide, Kristensen and Tsopanakis fall outside of the scope of the instant claims. Accordingly, Koide, Kristensen and Tsopanakis cannot anticipate the claimed invention, which requires a protein encoded by a nucleic acid having at least 90% identity to the nucleic acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

Finally, the Applicants respectfully submit that the claimed subject matter is limited to screening assays that involve "determining the amount of poly ADP-ribose produced by said *TaHo* protein" (i.e., a protein encoded by a nucleic acid having at least 90% identity to the nucleic acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2). Accordingly, even if Koide, Kristensen and Tsopanakis could somehow be construed as disclosing an assay using a purified mixture of different PARP proteins that includes TaHo, those references would still fail to teach all of the elements of the rejected claims

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Cir. 1999)

because they do not describe an assay directed to determining the PARP activity of the TaHo protein in particular.

The Applicants respectfully submit that this rejection has been adequately addressed. In view of the foregoing discussion, this rejection may be withdrawn.

Obviousness-type double patenting

Claims 27-30 and 38-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of USPN 6,589,725.

The Applicants submit herewith Terminal Disclaimers over USPN 6,589,725.

This rejection may be withdrawn.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-010CIP2.

Respectfully submitted,
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Date: March 10, 2004

By: _____
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Enclosures: Exhibits A-D

Terminal Disclaimer over USPN 6,589,725

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